

Attorney Docket No.: **UMD-0112**  
Inventors: **Alland and Hazbón**  
Serial No.: **10/540,460**  
Filing Date: **January 17, 2006**  
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**REMARKS**

Claims 1-7 are pending in the instant application. Claims 1-7 have been rejected. Claims 1 and 2 have been amended. Support for these amendments is provided in the specification at page 1, lines 13-16, page 4, lines 4-5, page 7, lines 33-35, Examples 3 and 7 and Figure 1. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

**I. Objection to Amendment to Specification under 35 U.S.C. 132 (a)**

The Examiner suggests that the amendment to the specification to include the priority claim introduces new matter as it contains the phrase "each of which are herein incorporated by reference." Further, the Examiner suggests that the correct international application no. is PCT/US03/41136, not PCT/US2003/041136. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the priority claim as suggested. Withdrawal of the objection is therefore respectfully requested.

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**II. Rejection of Claims 1-7 under 35 U.S.C. 112, second paragraph**

Claims 1-7 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner suggests that recitation of "primer-template matches" is indefinite.

Accordingly, in an earnest effort to advance the prosecution of this case and in accordance with teachings in the specification at page 7, Examples 3 and 7 and Figure 1, Applicants have deleted this phrase and amended claim 1 to recite comparing to a reaction containing a hairpin primer and a template with no mismatches.

The Examiner also suggests that the recitation of "the 30 to 90 base pair long amplicon of the nucleic acid sequence" renders claims 2-4 indefinite for lack of antecedent basis. Thus, in an earnest effort to advance the prosecution and in accordance with the Examiner's suggestion, Applicants have amended claim 2 to recite the 30 to 90 base pair long amplicon of the nucleic acid molecule.

Withdrawal of this rejection is respectfully requested.

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**III. Rejection of Claims 1-7 under 35 U.S.C. 112, first paragraph**

Claims 1-7 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner suggests that the specification as originally filed does not appear to provide basis for the concept of comparing the efficiency or threshold cycle or amount of amplified product in a reaction containing the short amplicon of 30 to 90 base pairs with any reaction "containing primer-template matches."

Accordingly, Applicants have amended the claims in accordance with teachings in the specification at page 7, Examples 3 and 7 and Figure 1 to recite comparing to a reaction containing a hairpin primer and a template with no mismatches.

Withdrawal of this rejection is respectfully requested.

**IV. Rejection of Claims 1-7 under 35 U.S.C. 103(a)**

Claims 1-6 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (U.S. Patent No. 6,090,552), as evidenced by Genbank Accession No. NM\_000025 in view of Matsuzaki (U.S. Patent No. 6,333,179), Metallinos (U.S. Patent No. 6,372,900) and Lopez (U.S. Patent No. 6,514,698).

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Claim 7 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko (U.S. Patent No. 6,090,552), as evidenced by Genbank Accession No. NM\_000025 in view of Matsuzaki (U.S. Patent No. 6,333,179), Metallinos (U.S. Patent No. 6,372,900) and Lopez (U.S. Patent No. 6,514,698) and further in view of Tyagi (U.S. Patent No. 6,365,729).

The Examiner has acknowledged that Nazarenko does not teach a method wherein the amplification product is of a length of 30 to 90 bp.

However, the Examiner suggests that Matsuzaki teaches that methods of PCR are more efficient when shorter length nucleic acids are amplified. The Examiner suggests that Lopez also teaches that methods that produce short PCR products of 30-100 bp provide several advantages. Finally, the Examiner suggests that Metallinos exemplifies methods of allele specific PCR in which the amplification products are of a length of 90 bp.

Applicants respectfully traverse this rejection.

It is respectfully pointed out that the instant invention relates to a modified amplification refractory mutation (ARMS) assay. Applicants have amended claim 1 in accordance with teachings at page 1, lines 13-16 and page 4, lines 4-5 of the instant specification to recite a modified amplification

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refractory mutation (ARMS) assay. The Background section of the instant application provides detailed teachings of the original ARMS assay. See pages 2-3 of the instant specification. At page 6-7 of the instant application, the modifications made to the assay in accordance with the instant invention as well the advantages achieved are set forth. Further, Examples 5 and 6 at pages 16-18 describe experiments wherein comparisons of the original ARMS with the modified ARMS of the instant invention showed superiority of the modified ARMS of the instant application. Specifically, the modified ARMS assay of the instant invention was demonstrated to have a much greater discriminatory power than the original ARMS assay. The original ARMS assay identified the correct SNP in only 7 of 13 assays (producing one incorrect and five indeterminate results), while the modified ARMS assay of the instant invention identified the correct SNP in all 13 assays. Also see Figures 2A and 2B, triangles. Furthermore, the modified ARMS assay of the present invention appeared to be more sensitive for SNPs as the ΔCt values were greater in the modified ARMS assay of the present invention compared to the original ARMS assay. See Table 2 at page 17 of the instant specification.

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The combinations of cited references do not teach or suggest the modified ARMS assay of the present invention.

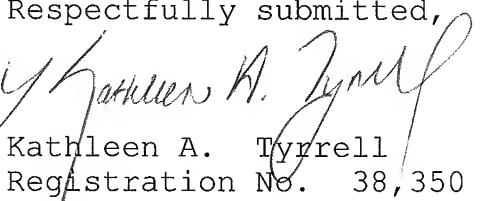
Further, MPEP 2141 and *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, 82 USPQ2d 1385 (2007) are clear; when considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* at \_\_\_, 82 USPQ2d at 1396. Here, the data clearly demonstrate superior properties in both accuracy and sensitivity of the instant claimed assay unexpected over any prior art teachings. Such results were clearly unpredictable to one of ordinary skill in the art from the cited prior art teachings. See MPEP 2143.01 and *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, \_\_\_, 82 USPQ2d 1385, 1396 (2007). Accordingly, the data provided in the instant specification of superior properties of the instant claimed invention rebuts any *prima facie* case of obviousness which has been asserted by the Examiner in the instant application.

Withdrawal of these rejections under 35 U.S.C. 103(a) is therefore respectfully requested.

**V. Conclusion**

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Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,  
  
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